**UNITED STATES DISTRICT COURT**
**FOR THE MIDDLE DISTRICT OF TENNESSEE**
**NASHVILLE DIVISION**

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| **RUTH SMITH, Individually and as Widow for The Use and Benefit of Herself and the Next of Kin of Richard Smith, Deceased,** | ) | |
| **Plaintiff,** | ) | **Case No. 3:05-0444** |
| **v.** | ) | **Judge Aleta A. Trauger** |
| **PFIZER INC., et al,** | ) | |
| **Defendant.** | ) | |

# REVISED EXPERT WITNESS STATEMENT OF DOUGLAS JACOBS, M.D.[1]

I am a psychiatrist from Boston, Massachusetts and I have been asked to address two questions in this case: first, whether there is any scientific evidence that Neurontin causes suicide; and second, whether Neurontin caused the suicide of Mr. Smith. For reasons I will discuss in detail, my opinion is that there is no reliable scientific evidence that Neurontin causes suicide in any individual or group of individuals. Further, my opinion is that Mr. Smith's suicide had nothing to do with Neurontin but instead is fully explained by his devastating experience with pain and the total deterioration of his body, leading to a state of hopelessness resulting in the choice of suicide as the only option rather than living with unbearable pain.

[1] This revised statement is being submitted in response to new studies cited in Dr. Maris's Direct Statement, pursuant to the Court's permission to submit such a statement. The new language is highlighted in redline herein.

**Qualifications**

I am an associate clinical professor of psychiatry at Harvard Medical School where I have been on the faculty since 1975. I graduated from the University of Pennsylvania School of Medicine in 1971 and completed a three-year residency in psychiatry at the Massachusetts Mental Health Center, which is a Harvard Medical School training program. I was board certified by the American Board of Psychiatry and Neurology in 1977, and remain certified today.

I have devoted my career to the study of and treatment of suicidal patients, as well as educating the public and colleagues regarding suicide assessment. I am the editor of an official textbook from Harvard Medical School, entitled, the Harvard Medical School Guide to Suicide Assessment and Intervention which was published in 1999. I have organized and led academic seminars both locally and nationally, that teach mental health professionals about suicide and related psychiatric subjects such as depression. In 1981 I founded the Harvard Medical School Suicide Symposium. In 2001, I received the highest honor in my career when I was appointed by the American Psychiatric Association to be the chairperson of the workgroup to develop the Practice Guidelines for the Assessment and Treatment of Patients with Suicidal Behaviors. Our work group published these guidelines in 2003 and 2004.

My clinical practice for the past 35 years has focused intensively on evaluating, treating, and consulting on suicidal patients. Between 1975 and 1983, I was the director of the psychiatric emergency services at Cambridge Hospital. At Cambridge Hospital, I was responsible for evaluating and supervising more than 3,000 psychiatric emergencies each year. In that patient population, we averaged approximately one suicide attempt

each day. This clinical experience with a variety of suicidal behaviors, particularly in a general hospital setting, enriched my understanding about the causes of suicide.

From 1986 through 1990, I consulted to the Hospital Corporation of America, here in Nashville, designing educational programs for the medical directors of the over 100 psychiatric hospitals which were owned by HCA at that time. I conducted two large programs in Nashville in 1986 and 1988. Currently, I am on the staff at one of the foremost psychiatric hospitals in the country, McLean Hospital in Belmont, MA.

Because of my expertise in the field of suicide, I am frequently referred patients at risk for suicide. In addition to treating individual suicidal patients, I am regularly asked by clinicians, hospitals, and school systems to provide consultation regarding the assessment of a suicidal patient or in the aftermath of suicide. The American Psychiatric Association regularly refers questions related to suicide from the media to me. I have also provided expert consultation on medical legal matters for both plaintiffs and defendants including cases involving allegations that individuals committed suicide as the result of alleged medical malpractice or due to the effects of a drug or substance. I have also testified twice before Congress; first, at the request of the House Armed Services Committee during its investigation of the explosion on the U.S.S. Iowa and whether or not a sailor committed suicide and homicide; and second, before the House Committee on Government Reform regarding a presentation I made before the FDA in 2000.

Because of my interest in the field of suicide and its relationship to depression I developed a program in the early 1990s entitled National Depression Screening Day, which is a national program that offers free mental health screenings to the public. National Depression Screening Day is endorsed by the American Psychiatric Association.

This developed into a non-profit organization – Screening for Mental Health (SMH). SMH has grown significantly over the past 20 years. It offers programs in middle schools, high schools, colleges, primary care offices, and hospitals. Importantly, we currently have a contract with the Department of Defense which provides screenings for all military personnel and their families. Our programs include both in-person and online screenings for Depression, Bipolar Disorder, Generalized Anxiety Disorder, Post-Traumatic Stress Disorder, Eating Disorders, Alcohol Programs and Suicide Prevention. In the past year we had 20 screening sites in the state of Tennessee. As part of my interest in educating colleagues on the assessment of suicide, I developed a protocol for the assessment of suicide, entitled the SAFE-T, which is a condensation of the work that I did on the Practice Guidelines. Recently, this card has been distributed to mental health clinicians in all branches of the military.

During my career I have received a number of awards including the Massachusetts Psychiatric Society's Outstanding Psychiatrist award in 2004 for the advancement of the profession, as well as a commendation from the Massachusetts House of Representatives in 2007 for my work on National Depression Screening Day.

A copy of my professional curriculum vitae, or CV, that lists more details about my education and experience is marked as Ex. 7444.

**Materials Reviewed**

I reviewed a great deal of material for this case. In terms of general causation, I have reviewed reports from Pfizer that have been presented to the FDA regarding the suicide events. I looked at data from the Neurontin clinical trials and Adverse Event

Reports, and the FDA's analysis of suicidality in studies of antiepileptic drugs, specifically, Neurontin. In terms of specific causation, I reviewed Mr. Smith's medical records, depositions of Mr. Smith's family, friends and treating physicians, as well as plaintiff experts in this matter, police records of the investigation into Mr. Smith's suicide, Mr. Smith's suicide note, and Plaintiff experts' reports. I have also reviewed the extensive literature that pertains to the articles published on Neurontin, pain and functional limitations and its relationship to suicide, and other relevant literature.

**Background on Suicide**

Suicide was in 2004 and continues today to be a significant public health problem. For a variety of reasons, including the problem of stigma, only 30% of persons who commit suicide are in active psychiatric treatment at the time. Suicide is the 11$^{th}$ leading cause of death in the general population in the United States with approximately 33,000 Americans dying by suicide each year. Suicide is a multi-factorial event, which means that a suicide is understood as the outcome of not one cause but rather a combination of multiple different factors. Importantly, no textbook from any professional organization, including the Practice Guidelines from the APA, peer-reviewed article, evidence based clinical study, nor the FDA analysis on the relationship between drugs and suicidality lists medication as a cause of suicide. It is known that 90-95% of persons who commit suicide suffer from a mental illness with depression being the prominent disorder found in patients who commit suicide.

Physical illness is also significantly associated with suicide with more than 25% of persons who commit suicide having a relevant physical illness. This percentage increases as age increases and for a person of Mr. Smith's age (over the age of 75) this

percentage reaches 70%. Let me repeat that – 70%. Furthermore, white males comprise the majority of suicides and individuals like Mr. Smith (over the age of 75) are at the highest risk for suicide. Physical illnesses such as chronic pain and functional limitations play a strong role in increasing the suicide risk, particularly in the elderly. Chronic pain syndromes have been identified as an independent risk factor for suicide, increasing the suicide risk by 2-3 times. Hopelessness is another key risk factor for suicide. Patients with a combination of depression and chronic pain with functional limitations are at the highest risk for suicide when they are confronted with the harsh reality that there is no hope for relief from their physical or emotional pain; suicide can become the only option to end the pain.

Finally, access to firearms is relevant since firearms are the most common method of suicide, particularly among elderly males. Risk factors can act synergistically, which means that the combination of the factors increase the risk more than simply adding them together. For that reason, a person like Mr. Smith, a 79 year-old white male who had access to firearms, who was depressed and had suicidal thoughts before starting Neurontin and had a long history of severe incapacitating chronic pain, and who had become hopeless about his physical and emotional condition would be considered to be at a high risk for suicide.

**General Causation**

There is no reliable scientific evidence that Neurontin causes suicide. There has been no study demonstrating that Neurontin causes suicide. The FDA, the regulatory authority that oversees pharmaceuticals, has not determined that Neurontin causes suicide. It is accepted in the field that it is the evaluation of controlled clinical trials that

forms the basis as to whether or not a medication causes an adverse outcome, such as suicide. The controlled clinical trial is an experiment where subjects are randomly divided into two groups, with one group given the medication under study and a similar group given an inactive substance called a placebo or sugar pill. By comparing the adverse events in the two groups, one can determine with some confidence whether the events seen in the patients receiving the active medication are the result of the drug. For example, patients with chronic pain like Mr. Smith are at increased risk for suicide regardless whether they take any medication. So one would expect a certain number of chronic pain patients who are given any medication to think about suicide, to make suicide attempts or even to commit suicide. But without comparing patients who are treated with a medication to a group of similar patients taking a placebo, it is not scientifically possible to conclude that the adverse events in the patients taking the medication are due in any way to the medication. Since it is known that chronic pain patients are at a higher risk for suicide, by including a control group of similar patients that is not receiving the medication, we can compare the rates of the events in the two groups to see if the drug makes a difference. For these reasons it is generally accepted in the medical and scientific community that data from placebo-controlled trials in randomized (i.e. similar) groups of patients, is the only basis upon which one can draw a reliable scientific conclusion about causation and not anecdotal reports. To repeat, there is no finding, from any clinical trial that Neurontin causes suicidal thoughts or behavior. For that matter, there is no study showing that any medication causes suicide, which is what this case is about.

Another concept that is important but at times challenging to understand is statistical significance. Briefly, statistical significance is the measure of how likely it is that the observed difference is real or caused by random chance. The basic example is flipping a coin. If you flip a coin multiple times, it is possible that the coin will come up heads each time due to random chance. Statistical significance measures the likelihood that a difference seen in the study is not due to that type of random variation but rather to a real difference in rate. Thus, in looking at the controlled studies, it is generally accepted by doctors and scientists that a non-statistically significant difference is not reliable scientific evidence of causation. Despite what you have heard about the FDA's meta-analysis of anti-epileptic drugs, if one looks specifically at Neurontin, which is the anti-epileptic drug in this case, the placebo controlled data for Neurontin do not indicate any increase in suicidal thoughts or actions in patients treated with Neurontin versus the placebo controlled group.

**[Demonstrative: June 22, 2006 Letter from Dr. Evertsz (Pfizer) to Dr. Katz (FDA)]**

In June of 2006 Pfizer provided a report to the FDA on suicide events in all of Pfizer's controlled trials in response to the FDA's request for information on anti-epileptic drugs and suicide. As the report states, in the table shown here, in the Neurontin trials, which involved 5,194 patients, importantly there were no patients who either committed or attempted suicide. Even looking at suicidal ideation, which is thinking about suicide, the rates were basically identical in the Neurontin and placebo treated patients. Specifically, .039% of Neurontin patients and .037% of placebo patients reported suicidal thoughts. Thus, there is no statistically meaningful difference between these rates, leading to the conclusion of no increased risk for Neurontin.

Furthermore the controlled trials provided no indication that Neurontin increased the risk of depression or anxiety. There have been at least 3 well-controlled trials studying Neurontin in patients with panic disorder, bipolar disorder and social phobia. Those studies use the gold standard method for measuring depression and anxiety referred to as the Hamilton Depression and Hamilton Anxiety rating scales. There was not any statistical difference between the Neurontin treated group and the placebo group in scores on either of those scales in any of the 3 studies meaning that Neurontin is not associated with, and does not cause or worsen, depression or anxiety. Importantly, the FDA alert does not state that the anti-epileptic drugs cause depression or anxiety. The alert was specific for suicidality, but as I said earlier, that individually this would not be true for Neurontin.

To summarize, the FDA's pooled analysis of controlled data on 11 different anti-epileptic drugs including Neurontin, which led the FDA to impose additional suicide warning requirements for all anti-epileptic drugs does not alter my conclusions. As I have said, that analysis did not find a statistically significant increase for Neurontin itself. Furthermore, the FDA did not find an established causal mechanism between any of the anti-epileptic drugs, much less Neurontin itself in suicidal thoughts or actions. I also rely on the analysis performed by Dr. Gibbons who demonstrated several additional reasons why the FDA's analysis does not provide reliable scientific evidence that Neurontin causes suicide.

A case report or anecdotal evidence is a description of a patient who developed an adverse event after being prescribed a medication. The FDA has repeatedly said that case reports are not to be used to imply causation. Case reports can generate a concern about

the safety of a drug but it is only with an evaluation of the placebo-controlled clinical trials that causation can be determined. For example, a patient treated with Neurontin may have a suicidal thought, attempt suicide or commit suicide which then gets reported to the company of the FDA. This type of information is regularly collected by companies like Pfizer and reported to the FDA, but there is no scientific way to determine whether the events reported were caused by the drug which is the position of the FDA. The only scientifically valid way to make the determination as to whether the adverse event was caused by a drug such as Neurontin and not by the reason for which Neurontin is being prescribed, such as chronic pain or mental illness, is to have a group of similar patients treated with placebo so that it can be determined whether the event occurred more frequently in patients on the drug. The FDA has repeatedly expressed the view that anecdotal evidence or case reports are not reliable for determining causation. As you have heard, since there is no evidence from the controlled clinical trials, the plaintiff experts rely on other kinds of information, such as mechanism theories, case reports, and studies with no placebo control group, none of which prove causation. To repeat, the FDA states unequivocally that case reports are not proof of causation.

Finally, the Plaintiffs' expert, Dr. Maris, cites two studies that compared Neurontin to one or more other drugs. But such drug-to-drug comparison studies do not answer the question that matters, which is whether the drugs actually cause suicide. Drug-to-drug studies only tell you how one drug compares to the other. It may be that neither one of them causes the problem. Imagine giving 100 patients aspirin and 100 patients Tylenol. Assume that the aspirin reduces fever better than Tylenol. You do not conclude from this that Tylenol causes fever. In one of the studies Dr. Maris cited,

bipolar patients treated with lithium had less suicide than those treated with Neurontin. That's not surprising, because lithium reduces suicide risk in bipolar patients, much like aspirin reduces fever. That tells us nothing about whether Neurontin causes suicide. To test causation, scientists have to do a different kind of test. They have to compare the risk in patients who take a medication to the risk in patients who take no medication. That is the right kind of test to answer the question of causation. The best way to do that kind of test is to use a placebo control group -- to compare what happens to patients who take the medication to patients who take a lookalike, but chemically inactive sugar pill. Those are the kinds of studies that FDA, for example, requires drug companies to use to prove the beneficial effects and the side effects of medicines. Those are the right kind of studies to answer the causation question; the ones Dr. Maris cites are not. In addition, I agree with Dr. Gibbons's opinions about the limitations of drug-to-drug comparison studies.

To briefly summarize my opinions, there is absolutely no reliable scientific evidence that Neurontin causes suicide.

**Opinions on the Cause of Mr. Smith's Suicide**

In my professional career, dating back to 1972 which encompasses my clinical, consultative and medical legal practice I have evaluated over 1,000 suicides. The overwhelming majority of them involved a person suffering from unbearable pain, either emotional, physical or both, that became intolerable resulting in them taking their own life. It is tragic for the person, as well as for the surviving family. The suicide of Richard Smith is no different.

**[Demonstrative: Mr. Smith's Pain Complaints]**

As shown in this chart titled "Mr. Smith's Pain Complaints," the medical records clearly document that Richard Smith suffered from bone, joint, and spine abnormalities which resulted in both pain and replacement surgery.

**[Demonstrative: Mr. Smith's Surgeries]**

As shown on this timeline titled "Mr. Smith's Surgeries," numerous joints in his body had been either operated on or replaced. Within the span of 10 years, he had 2 knees replaced, 1 hip replaced, and a spinal fusion operation.

As can happen with persons who experience pain over an extended period of time, Richard Smith developed depressive symptoms. These symptoms escalated to the point where he had two documented episodes of suicidal ideation prior to his use of Neurontin.

**[Demonstrative: February 27, 2003 Neurological Surgeons Questionnaire]**

In a patient questionnaire filled out by Mr. Smith on February 27, 2003, during a visit to Neurological Surgeons, Mr. Smith reported that he was "depressed due to pain and lack of sleep." This is more than a year before he first uses Neurontin.

**[Demonstrative: May 2, 2003 Neurosurgical Associates Notes – Dr. McCombs]**

As shown in a May 2, 2003 note, also from Neurosurgical Associates, just two months later, on May 2, 2003, his daughter told his providers that Mr. Smith "wished he could die because of pain and depression." Two weeks later, he was diagnosed with

depression by his primary care doctor and treated with an antidepressant, Lexapro. All of this was before he ever ingested any Neurontin.

Living with chronic pain requires pain coping strategies but we all have our limits. When pain coping strategies begin to fail, pain catastrophizing can develop, which in plain language means that ones mind and body are consumed by the experience of pain (this is echoed in the suicide note of Richard Smith which we have heard about). When this type of catastrophizing develops, it has been demonstrated that suicide risk further increases. By January of 2004, Richard Smith had become consumed by pain. He visited multiple doctors and had multiple tests.

**[Demonstrative: May 13, 2004 Police Report]**

According to the police report, family members told police that during this period he had a second episode of suicidal ideation, on March 1, 2004. During the last six weeks of his life, he saw multiple doctors, and he was told that he was not a candidate for surgery. As I will explain from Mr. Smith's records, surgery had always been his one last hope; it had fixed his aching body on numerous occasions providing a return to function or a relief from pain.

**[Demonstrative: March 31, 2004 Dr. McCombs's Notes]**

The record of Mr. Smith's March 31, 2004 office visit with his spine surgeon, Dr. McCombs, shows that Mr. Smith was told on March 31, 2004 that this was no longer possible. He was 79, in great pain, and told he could no longer have surgery to try to help his pain. Richard Smith reported to his dentist 3 days before his suicide that he was

experiencing hopelessness regarding whether there would ever be an end to his pain. He was also feeling useless. These are classical risk factors for suicide.

**[Demonstrative: Suicide Note]**

As we see in this enlargement of his suicide note, the suicide note explains the critical role of pain and how it had infected his mind and body. The suicide note is a classic example of pain catastrophizing where he states, "forgive me, I cannot go on like this." There is a direct correlation between the impact of pain and the suicidal state. Unfortunately, Richard Smith was not "a well man," as the Plaintiff's experts' state incorrectly, and his suicide was certainly not impulsive. Well recognized risk factors fully explain Mr. Smith's suicide without regard to Neurontin. In my opinion as a psychiatrist and suicidologist, to a reasonable degree of medical and scientific certainty, it was these multiple factors that led to Mr. Smith's suicide and not Neurontin. I do not believe Neurontin was a cause, or even a contributing factor, in Mr. Smith's suicide. Neurontin was simply one of many medications that had been prescribed to try to help him before his suicide during the last several years of his life.

Even if I assumed that Neurontin increased suicide risk in some patients, I believe Mr. Smith's suicide was not the result of Neurontin, but the result of the combination of several well-recognized risk factors for suicide. Specifically these factors include Mr. Smith's pre-Neurontin depression and suicidal thoughts, his chronic and severe pain and functional limitation, his status as an elderly white male with ready access to a firearm,

and the hopelessness brought about by being informed that he had no options left to treat his unremitting pain.

**[Demonstrative: Mr. Smith's Diagnoses]**

Mr. Smith's medical history, specifically his battle with pain, is central to understanding his suicide. This chart summarizes Mr. Smith's diagnoses from 1987 on. The diagnoses highlighted in yellow indicate pain problems. A review of Mr. Smith's medical records reveals an extensive history of physical complaints, degenerative, arthritic, and bone disorders, dating back to the late 1980s that led to chronic pain with the gradual and steady deterioration of his entire body. As early as 1989 he was diagnosed as having degenerative joint disease in his right knee. By 1992 the knee pain had progressed to where he now had degenerative arthritis in both his knees. This progressed to the point where he had his left knee replaced in 1993, something which was not very common back then. However, he did get relief and physical therapy was noted to be helpful. This is important to keep in mind about the relief surgery provided for Mr. Smith because in 2004 Mr. Smith was told that he was no longer a candidate for surgery. Over the next 10 years nearly every major joint was either replaced or afflicted with unbearable pain. In the mid 90s, in addition to his right knee, he developed pain in his right hip due to severe arthritis and was told he would have to have his right hip replaced. Thus by 1998 Richard Smith had had both knees and a right hip replaced. Although he returned to work after these surgeries, it was only on a half-time basis. I mention this because one of the plaintiff experts, Dr. Trimble reported that Mr. Smith continued to work full time up until his suicide. Although this may seem like a small matter, this is

important because of the plaintiff experts' assertion that Mr. Smith was a healthy man and that his failing body did not impact his life.

**[Demonstrative: Mr. Smith's Pain]**

As shown in this chart titled Mr. Smith's Pain, by 2004, Mr. Smith had serious pain problems in virtually every part of his body. Even the simple pleasure that Mr. Smith said he got from cutting the grass was taken away from him. As was noted in the records in 2003 and 2004, Mr. Smith's unremitting pain had progressed to the point where he was no longer able to cut the grass or perform other physical activities.

**[Demonstrative: Mr. Smith's Prescriptions]**

The medication records and history tell us a lot about the pain that Richard Smith experienced over the years. Pain medications were first prescribed in the early 1990s and became regular by 2000. As shown in this chart, titled "Mr. Smith's Prescriptions," in the last 6 years of his life, Mr. Smith had been prescribed 20 different pain medications from virtually every class of pain medicines. Again, this is noteworthy since the plaintiff experts only refer to the last 12 months of Richard Smith's life and its relationship to pain medications. The important point is that Mr. Smith's doctors had prescribed many, many medications to try to relieve his pain, and no one medication or any combination had adequately relieved his pain.

As if the pain in Richard Smith's hips, and knees was not bad enough, in 2001 and 2002 Mr. Smith was diagnosed with more painful conditions. He suffered a tear in

the rotator cuff which led to pain under his shoulder, torn biceps, and he was also diagnosed for the first time with degenerative joint disease of the spine. This tear in the rotator cuff which again might be incidental for us, is significant here, because it is the rotator cuff which is referred to in Mr. Smith's suicide note. Furthermore at this time, more difficulties were noted by Mr. Smith's doctors in which there is now evidence of neck pain, chest pain, vertigo and poor sleep. Poor sleep or insomnia is relevant given that insomnia is also a risk factor for suicide. If this wasn't enough for one person to bear, at this time, Mr. Smith's primary care doctor, Dr. Cato, began to consider the diagnosis of fibromyalgia. Fibromyalgia is a total body illness that is highlighted by chronic and widespread pain and is associated with impairments of memory and concentration and comorbid (or accompanying) psychiatric conditions, such as depression and anxiety. This was evidenced by Dr. Cato's prescription of Amitriptyline which is the standard treatment for fibromyalgia when there are sleep disturbances and symptoms of depression. Interestingly, Mr. Smith was also recommended to start Neurontin, which is a recommended treatment for fibromyalgia, although he did not fill the prescription at that time. Although Mr. Smith was not formally diagnosed with depression until nearly 2 years later by Dr. Cato, it is notable that fibromyalgia patients commonly experience depressive symptoms.

By 2002 even the replaced joints began to cause Mr. Smith pain. In 2003 the progression of bodily deterioration continued. He developed neurologic symptoms related to his back injury, including decreased reflexes, weakness, numbness and tingling. His sleep became severely impacted. Here in 2003, we begin to see the pain causing a deterioration of his mood.

**[Demonstrative: February 27, 2003 Neurological Surgeons Questionnaire]**

Importantly, as shown in the February 27, 2003 Neurological Surgeons Questionnaire filled out by Mr. Smith during a doctor's visit, Mr. Smith noted, more than one year before he first took Neurontin, that he was "depressed because of pain and lack of sleep."

**[Demonstrative: February 27, 2003 Dr. Berklacich's Notes]**

Also, as shown in a February 27, 2003 note of the visit recorded by Dr. Berklacich, at this same time, February 27, 2003, Mr. Smith rated his pain as severe, an 8 on a 0-10 scale. Again, this is significant because this is the same level of pain that Mr. Smith recorded over a year later, just 4 days before his suicide. Even the basic function of walking was afflicted in which he was noted to have difficulty walking due to weakness and that standing, walking, coughing, sneezing, prolonged sitting and even lying down made his pain symptoms worse. His pain was not improved by any type of movement or re-positioning. Imagine what it would be like to be afflicted by pain and not be able to get any relief no matter what you did. By this point, Mr. Smith was taking both pain and sleeping pills. He reported that pain awakened him during the night and that the pain pills really did not help. He was even forced to undergo epidural steroid injections. This type of injection is when a needle is basically put into the back of your neck in the spine area. He had to endure these injections; but even those did not give him significant relief of his symptoms.

**[Demonstrative: March 5, 2003 Mrs. Smith Phone Call to Dr. Berklacich]**

In a March 5, 2003 phone call by Mrs. Smith to Dr. Berklacich's office, Mr. Smith's severe pain was noted by his wife, as she reported to one of the doctors, "I don't know what's wrong with Richard, he is in so much pain, he is out of his mind."

Even though Mr. Smith was reluctant to have another surgery, he finally agreed to have surgery on his back because he "was in so much pain." In April 2003 he underwent extensive back surgery called a decompressive lumbar laminectomy. Unfortunately this surgery was not successful in alleviating Mr. Smith's pain. Within one month of the surgery he again complained of back and leg pain and was placed on narcotic pain medication.

**[Demonstrative: May 2, 2003 Neurosurgical Associates Notes – Dr. McCombs]**

As shown in this May 2, 2003 Neurological Associates note, the pain and frustration mounted to the point where Mr. Smith let his daughter know, who in turn appropriately reported it to Mr. Smith's doctor that, "he wishes he could die because of pain and depression." Thus, at least one of his daughters was aware in 2003 that Mr. Smith's pain had progressed to the point of suicidal ideation, and this was a year before he first used Neurontin. Appropriately, Mr. Smith's doctor recommended a psychiatric evaluation; but Mr. Smith never followed through on this evaluation. Would involvement of a psychiatrist at this point in Mr. Smith's battle with pain and depression have made a difference in the ultimate outcome? Of course, we will never know, but I want to be clear that I'm not blaming Mr. Smith or his family for not obtaining a psychiatric evaluation. It is not unusual for patients, particularly the elderly, to refuse psychiatric care because of the underlying stigma about seeing a psychiatrist. Like three quarters of the 30,000 people who commit suicide each year, Mr. Smith's depression and

suicidality, evident a full year before he died and long before he used Neurontin, went untreated.

Mr. Smith's statement in 2003 that he wished he could die because of pain and depression is significant for a number of reasons. First and most importantly, this statement is an example of suicidal ideation and it occurred 10 months before he ingested any Neurontin. Mr. Smith's experience of suicidal ideation in response to the pain he was experiencing in May of 2003 is very significant because he experienced the same or worse symptoms and degree of pain in 2004 which again produced his second episode of suicidal ideation. This second episode of suicidal ideation is documented in the police records where Mr. Smith's daughter Cindy Smith reported that on March 1, 2004 Mr. Smith again had experienced suicidal ideation. This is the second episode of suicidal ideation before Mr. Smith ingested any Neurontin. So on at least two documented occasions before he ever used Neurontin, Mr. Smith thought about the option of suicide. This is compelling evidence that Mr. Smith's suicide was precipitated by the reality that he was no longer going to be able to find relief from his severe pain.

To return to 2003, in May, Dr. Cato diagnosed Mr. Smith with depression, the number one disorder associated with suicide. Dr. Cato noted that Mr. Smith had depression and anxiety as well as "having a lot of pain." Dr. Cato prescribed two anti-depressants; Lexapro and desipramine. The Lexapro was specifically prescribed for depression and anxiety. Dr. Maris contends that Mr. Smith was never prescribed a psychotropic drug. This is of course incorrect in that both Lexapro and desipramine are psychotropic drugs. So, not only had Mr. Smith experienced suicidal ideation before Neurontin, but he was also diagnosed with depression before he ingested any Neurontin.

Mr. Smith's already deteriorating condition further deteriorated in 2004. He was noted for the first time to have increased blood pressure, which can develop in response to severe pain and stress. 2004 is significant for another reason; Mr. Smith began a process of doctor shopping. He saw two doctors, Dr. Shell and Dr. Mackey, in consultation for the pain. It is during this period of increased pain and multiple doctor visits that Mr. Smith reported the suicidal thoughts to Cindy Smith on March 1st. He was now even noted to have degenerative changes in his wrists and shoulders. No body part was spared.

**[Demonstrative: March 9, 2004 Dr. Mackey's Notes]**

A March 9, 2004 visit with Dr. Mackey indicates that Mr. Smith reported knee pain and worsening pain in both of his legs. The pain had increased to the point where Mr. Smith was now using a wheelchair, at least as observed in Dr. Mackey's office. The possibility of surgery was discussed. During this visit, as shown in Dr. Mackey's March 9, 2004 office record, Mr. Smith's daughter "raised the concern about whether or not there are some other issues going on and that we (the family) are going to go ahead and have him evaluated psychiatrically to make sure that there is not a dementia type issue playing into this as well." This is a very important event. First, this visit and these observations are before Mr. Smith used Neurontin. Second, "Dementia" means an impairment of loss of mental faculties, like loss of memory or executive functioning.

Mr. Smith had a number of reasons to have had changes in his cognitive status, or ability to think. First, Fibromyalgia can cause impairment in memory and concentration. Secondly, Mrs. Smith had noted that Mr. Smith's level of pain caused him to be "out of his mind." Thirdly, depression itself can impair concentration. In fact, in the elderly, one

of the differential diagnoses for dementia is depression. Unfortunately for the second time, Mr. Smith and his family did not follow through with the psychiatric evaluation. I want to emphasize that I am in no way being critical of Mr. Smith or his family because even in 2010, many people are still reluctant to see a psychiatrist.

It was during this March 9th visit that the doctor prescribed Neurontin. Neurontin was prescribed as a non-narcotic medication that has been found useful in relieving chronic pain in some patients. It is important to note that there is no evidence in the records that the Neurontin had an impact on Mr. Smith's psychological symptoms such as his depression, anxiety or cognitive state.

On March 24, 2004, Mr. Smith visited Neurosurgical Associates "at the request of his wife." He reported pain in both of his legs that radiated down to his buttocks and groin, the interior part of his thigh and down to his knee. Mr. Smith attempted to see another doctor, Dr. Howell. This is significant as a sign of Mr. Smith's desperation to find relief at this point, in that he was apparently doctor shopping in an attempt to find a doctor who could alleviate his pain.

**[Demonstrative: March 29, 2004 Dr. Mackey's Notes]**

In a March 29, 2004 note, Dr. Mackey made reference to the issue of doctor shopping and recommended that Mr. Smith return to the original surgeon, Dr. McCombs for further discussion about possible surgery. During this timeframe, Dr. Howell, who Mr. Smith had just seen, now was refusing to see Mr. Smith further because of the doctor shopping.

**[Demonstrative: March 31, 2004 Dr. McCombs's Notes]**

It is this next visit on March 31, 2004 that was to serve as the catalyst for the eventual suicide. Dr. McCombs's record of the visit shows that, after evaluating a number of medical tests, Dr. McCombs determined that "he is not a candidate for any type of operative intervention. He will be treated conservatively." In my opinion, that was essentially the last straw – he was out of options, and became hopeless. Mr. Smith was told (according to Mrs. Smith) that he would "simply have to learn to manage his pain." This was not an unfeeling statement by Dr. McCombs but rather an occasion when doctors have to deliver bad news. There is a limit to our interventions. Imagine what Mr. Smith must have felt like at this point. In essence he was told that there was nothing more doctors could do for him to alleviate his severe pain other than this conservative treatment.

**[Demonstrative: May 5, 2004 Dr. McCombs's Notes]**

Over the next five weeks, Mr. Smith received no relief from his pain. As shown in Dr. McCombs's May 5, 2004 office note, on May 5, 2004, about 8 days before he suicided, he contacted Dr. McCombs office complaining of pricking and sticking feelings in his buttocks and legs. He indicated that he was taking Advil, Neurontin, and Lortab, an opioid, with no relief. He was receiving physical therapy but this was also of no help. Additional epidural steroid injections were recommended, but Mr. Smith stated in a handwritten note that he was discouraged that this was all that was being recommended for him. Although he would get temporary relief from physical therapy visits, by May 6, 2004, it is noted in the physical therapy records that there was no change in his severe pain. There are no further medical visits after this date. There is a visit to a dentist, a Dr. Christopher Woods, on May 10, 2004, who wrote a letter after Mr. Smith's suicide in

which he indicated that Mr. Smith referred to hopelessness, his attempts at getting second opinions, and his feelings of uselessness.

During the same period, Mr. Smith also was dealing with his daughter's terminal cancer illness. The transcript of Mrs. Smith's 911 call the morning of May 13, 2004, shows that, in addition to referring to Mr. Smith's pain and illness, Mrs. Smith noted that "our youngest daughter's been suffering with cancer and it's been . . . This has been too much, too much . . ." Mrs. Smith also said that Mr. Smith indicated that "he couldn't face the fact that his daughter had cancer and would die . . ." As Mrs. Smith recognized, his daughter's illness was another stressor that further compounded his depression and hopelessness.

**[Demonstrative: Suicide Note]**

Mr. Smith committed suicide on May 13, 2004 by gunshot. His suicide note stated the following: *"Pain has taken over my mind and body. I need back surgery, left and right rotator cuffs, right bicep torn, back surgery to correct pain in legs. Forgive me; I cannot go on like this. I cannot have my body, the temple of the Holy Spirit, cut on any more. I have talked to God all night and He understands."* This note explains the cause of Mr. Smith's suicide. Pain is the culprit, not Neurontin. Listen to his words, "Pain has taken over my mind and body…I cannot go on like this." Yes, Mr. Smith was a religious man. Even in the last moments of his life, completely in character, he was thinking about God. I searched the Bible for the reference in his suicide note and found 1st Corinthians, Chapter 6, Verse 19-20, which of course refers to the body as "a temple of the Holy Spirit." Certainly Mr. Smith is quoting from the Bible at this point. He spent some time praying to God and in a sense he was asking forgiveness and concluded that,

"He understands." This is not only a powerful statement but also a statement of a man who was in excruciating pain. Suicide notes are found in about 25% of persons who commit suicide. Suicide notes are inconsistent with impulsive suicide. This note, particularly, indicates that Mr. Smith spent time thinking about his suicide and praying to God. Also, the physical consequences of the suicide where he put a sheet over the bed and locked the door indicate the thought and planning of the suicide, rather than an impulsive, out of character, and unexplainable act.

To recap, the chronology of events provides the key to understanding Mr. Smith's suicide. Mr. Smith had suffered from bone, joint, and spine disease which resulted in both pain and replacement surgeries and functional limitations. Almost every joint in his body had either been operated on or replaced. These symptoms escalated to the point where he became depressed and had two documented episodes of suicidal ideation before he was prescribed Neurontin. He was treated with an antidepressant, Lexapro, before being prescribed Neurontin. By 2004, Mr. Smith's pain was severe and unrelenting and his doctors told him that there were no surgical options left. Basically, Mr. Smith could no longer tolerate the chronic pain. It is not only that he believed that the pain would never get better; he was not given any hope that it would. Although there had been an appointment scheduled with another surgeon, Mr. Smith indicates in his suicide note that he had had enough.

Mr. Smith became hopeless after March 31, 2004 not because of Neurontin but because of being told that he would simply have to live with the pain. Patients become suicidal in response to pain and depression when they have to confront the stark reality

that there is no hope for alleviation of their physical and emotional pain. Hopeless patients begin to view suicide as the only option to alleviate their pain.

It is apparent from the sequence of events leading up to his death as well as Mr. Smith's statements in his suicide note, that this is precisely what happened. Thus, it is my opinion as a psychiatrist and suicidologist, to a reasonable degree of medical and scientific certainty it was these multiple factors that led to Mr. Smith's suicide and not Neurontin.

**Response to Opinions of Dr. Trimble and Dr. Maris**

I disagree with the opinions of Dr. Trimble and Dr. Maris both in the matter of general causation and specific causation. In terms of Dr. Trimble and general causation, I disagree that there is scientific evidence that Neurontin causes suicide. I disagree with Dr. Trimble's reliance upon the FDA meta-analysis as proof that Neurontin causes suicide. In fact, the FDA meta-analysis does not conclude that anti-epileptics are associated with suicide. Furthermore, the FDA meta-analysis pertains to 11 medications. When these 11 medications are considered separately, there is no evidence that Neurontin specifically causes suicide nor had a statistically significant increase in suicidality. Dr. Maris bases his specific causation opinion on Dr. Trimble's general causation opinion with which I disagree.

In terms of specific causation, Dr. Trimble and Dr. Maris are actually at odds. Dr. Trimble opines that Mr. Smith had no risk factors for suicide. Dr. Maris on the other hand opines that Mr. Smith did have risk factors for suicide. Importantly, Dr. Maris acknowledges that prior to Neurontin, Mr. Smith had both depression and suicidal

ideation. As noted, Dr. Cato diagnosed depression and anxiety in Mr. Smith and prescribed the anti-depressant Lexapro 10 months before Mr. Smith started using Neurontin. Dr. Trimble's confusion on this issue apparently is at least in part due to the fact that he did know until his deposition that Lexapro was an anti-depressant. The medical records are clear on the existence of depression in Mr. Smith prior to Neurontin. The medical records indicate that Mr. Smith experienced depressed mood, insomnia, fatigue, diminished ability to think, and recurrent thoughts about suicide. These five symptoms satisfy the textbook diagnosis of Major Depressive Disorder. As previously stated, Major Depressive Disorder is the number one psychiatric illness associated with suicide.

In terms of the suicidal ideation, Dr. Trimble chose to ignore Cindy Smith's statement about the March 1, 2004 episode of suicidal ideation. Dr. Maris on the other hand wants to claim that it is, "a different kind of suicidality after Neurontin." As previously stated, there are two documented episodes of suicidal ideation, pre-Neurontin. For that reason, Dr. Maris and Dr. Trimble's claim that suicidal thoughts did not appear until after Neurontin was started is simply false.

Dr. Trimble also incorrectly opines that Mr. Smith's suicide was impulsive. There is extensive evidence that Mr. Smith's suicide was planned rather than impulsive, including the following: one, Mr. Smith had suicidal thoughts relating to his pain dating back to at least May 2003; two, Mr. Smith communicated to Mrs. Smith at least three week prior to his suicide, that he wondered what God would think if he committed suicide; three, Mr. Smith wrote in his suicide note that he had "talked to God all night" about his suicide, showing that Mr. Smith contemplated suicide for at least several hours;

four, the very fact that Mr. Smith wrote a suicide note shows planning as opposed to impulsiveness; and five, Mr. Smith was fairly meticulous in carrying out his suicide, locking the bedroom door and even laying down plastic to avoid soiling the bed. All of this evidence disproves Dr. Trimble's conclusion that Mr. Smith's suicide was impulsive. It is my opinion that Dr. Trimble's assertion that Mr. Smith's suicide was impulsive overlooks the psychological explanation for Mr. Smith's suicide. Mr. Smith's suicide was not an impulsive act occurring out of the blue but rather the culmination of a 20 year battle with bodily deterioration, functional limitation, and severe and incapacitating pain. This culminated in a state of hopelessness.

Dr. Trimble and Dr. Maris both concede that hopelessness contributed to Mr. Smith's suicide, but they incorrectly attribute Mr. Smith's hopelessness to Neurontin. There is no scientific support for the assertion that Neurontin can cause hopelessness. Hopelessness is not listed as treatment emergent event that has been associated with Neurontin and there is no peer-reviewed literature suggesting an association between Neurontin and hopelessness. The FDA alert does not state any finding that the anti-epileptics in general or Neurontin specifically can cause hopelessness. As stated above, the clear and obvious explanation for Mr. Smith's hopelessness is the fact that he was suffering chronic pain and was faced with the specter of no relief from the treatments that he was receiving; being told by his doctor shortly before his death that there were no other treatment options available was simply too much for him to bear.

In terms of religion, both experts note that religious faith is a protective factor against suicide. Although I concur with this statement, it is important to point out that people with protective factors do commit suicide. In fact, many people who commit

suicide have both protective factors and risk factors present in their lives. For example, mothers with young children, people with positive social support, and people of faith, including Catholics, Jews, and Protestants, do in fact commit suicide. Mr. Smith had two episodes of suicidal ideation before Neurontin. When he became hopeless during the periods of March and April of 2004, he prayed to God in hopes that God would understand how the option of suicide had become his only choice. Ultimately, as his suicide note depicts, Mr. Smith believes that finally God understood. Thus, it was not that Neurontin changed Mr. Smith's attitude, or that it caused Mr. Smith to overcome strong religious prohibitions against suicide, but rather the unbearable state that Mr. Smith saw himself in and as he described in his visit to Dr. Woods, he saw no end to his pain. This is when people commit suicide, even if they are religious.

I disagree with Dr. Maris' view that Mr. Smith did not commit suicide because of chronic pain. Dr. Maris' reasoning that Mr. Smith lived for years with chronic pain but did not become suicidal until he took Neurontin is simply wrong. First, Mr. Smith was suicidal on at least two occasions before he took Neurontin. Secondly, and most importantly, Dr. Maris fails to appreciate that Mr. Smith's pain was fundamentally different in 2004 and that for the first time, surgery was no longer an option to relieve the pain. Mr. Smith had not been in that intolerable situation at any time in his life. It is understood in the science of establishing causation, that a 'temporal association,' between a medication and an outcome, that is the timing or taking of a medication and an event occurring, does not mean that the medication caused the suicide. There are other elements that have to be considered. It is critical to rule out bias and/or alternative explanation. It is clear what the alternative explanation is in the unfortunate suicide of

Richard Smith. It is his battle with pain and him being told that no longer could surgery relieve it.

Dr. Maris also claims that Neurontin changed Mr. Smith's positive attitude. Again, there is no science to support this statement. There is no basis for this statement from the clinical trials, nor from the FDA alert. In fact, there are multiple references in the record about how Mr. Smith's attitude about pain was impacted by the severity of the pain. He either wished he could die or that he was depressed because of it. This is in no way to criticize Mr. Smith but rather to appreciate the devastating impact that pain was having on his mood and wish to die.

In the pre-trial documents that I have reviewed, Dr. Maris had submitted a psychological autopsy form. I am highly critical of Dr. Maris's claim that this was supposed to provide scientific evidence concerning the cause of Mr. Smith's suicide. First, it was revealed in discovery that this form was filled out not by Dr. Maris, but by a legal assistant in the Plaintiff attorney's firm. This is totally unacceptable. During Dr. Maris's pre-trial deposition he attempted to correct some of the inaccuracies and omissions. For example, the form indicates that Mr. Smith was not prescribed any psychiatric drugs, yet the record is clear, Mr. Smith was prescribed Lexapro for depression before starting Neurontin. The form indicates that Mr. Smith did not have any psychiatric diagnosis prior to starting Neurontin; again, this is simply incorrect. Dr. Cato diagnosed depression in May of 2003, again, before Neurontin. The form does not acknowledge that Mr. Smith had pre-Neurontin suicidal ideation. Finally, the form does not make reference to Mr. Smith's pre-Neurontin history of depressive symptoms. In

short, Dr. Maris's psychological autopsy was inaccurate, incomplete, but most importantly, unscientific.

In summary, Mr. Smith's suicide was due to a combination of well recognized risk factors for suicide that tragically converged in 2004 to lead to his death. These risk factors included chronic pain, depression, pre-existing suicidality, being an elderly white male, and access to firearms. In 2004, Mr. Smith was told that he was no longer a candidate for surgery. This simply was too much for Mr. Smith to bear. Hopelessness mounted and the pain overwhelmed him. Mr. Smith's suicide note dramatically sums up these factors and explains the reasons for his suicide. "Pain has taken over my body…Forgive me; I cannot go on like this." There is no mystery why Mr. Smith chose to end his life. He left a note telling us why. It had nothing to do with Neurontin.

Respectfully submitted,

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**CERTIFICATE OF SERVICE**

I hereby certify that on this the 27th day of April, 2010, I electronically filed the foregoing document with the Clerk of the Court, United States District Court for the Middle District of Tennessee, using the CM/ECF system. True and correct copies of the foregoing documents are being served via the Court's CM/ECF system on the following:

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